## Preventing Antibiotic Resistance in the Wild

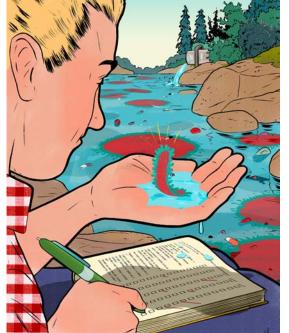
A New End Point for Environmental Risk Assessment

Human and veterinary antibiotics enter the environment through wastewater effluent, agricultural use of manure and treated sewage for fertilizer, and leakage from waste storage facilities. This antibiotic pollution may exert selective pressure on bacteria to develop drug resistance, which is especially concern-

ing if it develops in pathogenic bacteria. A new study weighs known bacterial antibiotic sensitivities against the backdrop of antibiotic concentrations measured in the environment and suggests that resistance in clinically relevant bacteria may not be kept in check by current risk assessment action levels [EHP 120(8):1100–1106; Tello et al.].

Ciprofloxacin, erythromycin, and tetracycline were selected for the analysis from among the approximately 150 compounds for which minimum inhibitory concentrations (MICs) have been reported for different bacteria. An MIC is the amount of antibiotic needed to inhibit bacterial growth. Each of the three antibiotics affects a wide range of bacteria and represents a distinct class of antibiotics used in humans and animals. Concentrations of each antibiotic in various environmental compartments, or media, had been documented previously.

Current guidelines for environmental risk assessment reflect the phase I action limits of the International Cooperation on Harmonisation of Technical Requirements for Registration of



Veterinary Medicinal Products. This program, which evaluates the safety of veterinary drugs, calls for environmental risk assessment of antibiotics whose concentrations exceed 1 ppb in aquatic compartments or 100 ppb in terrestrial compartments. These guidelines have been implemented in regulations in the United States, Europe, Japan, and Australia

The researchers compared information on antibiotic levels in the environment with information on the MICs of clinically relevant bacteria to determine if current levels of antibiotic pollution might be high enough to promote the development of resistance. Within aquatic compartments, only a small fraction of the 27 bacterial genera included in the study were predicted to be affected

by environmental concentrations of antibiotics, and results suggested that the phase I action level would protect against resistance. However, current levels of antibiotic pollution in terrestrial compartments—particularly in river sediments, liquid manure, and farmed soil—may be high enough to favor the evolution of bacterial resistance.

The conclusions may be limited by long-term selective pressure and by the fact that MIC tests do not represent environmental conditions. Furthermore, the authors did not address bioavailability or the potential influences of antibiotic mixtures, metals, or disinfectants. Nevertheless, the potential for antibiotic pollution to increase antibiotic resistance in clinically relevant bacteria has important implications for public health and environmental health policy, and the authors demonstrate a possible framework for answering important outstanding questions about the environmental impact of antibiotics.

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## What a Difference a Day Makes Examining the Lag Patterns of PM<sub>2.5</sub> Constituents

Exposure to fine particulate matter ( $PM_{2.5}$ ) is associated with a number of adverse health conditions, including cardiovascular and respiratory ailments, but less is known about associations with its specific chemical constituents. Past studies on the short-term effects of  $PM_{2.5}$  constituents have relied on data from monitoring networks that sample every third or sixth day. Now researchers report their findings on the daily lag patterns between exposure to individual  $PM_{2.5}$  constituents and hospital admissions for various conditions [*EHP* 120(8):1094–1099; Kim et al.].

 $PM_{2.5}$  is a complex mixture of water droplets and solid particles of carbon, nitrate, sulfate, metals, trace elements, and other constituents. In this study, researchers used information provided by the Denver Aerosol Sources and Health (DASH) study, which measured  $PM_{2.5}$  constituents daily for five years (2003–2007) in the Colorado capital. They focused on four of the main constituents of  $PM_{2.5}$ —elemental carbon (EC), organic carbon (OC), sulfate, and nitrate.

The researchers obtained data on discharge diagnoses following nonelective hospital admissions (e.g., emergency, urgent, or trauma care) in the five-county Denver metropolitan area. They categorized cardiovascular diagnoses as ischemic heart disease, congestive heart failure, or cerebrovascular disease, and respiratory diagnoses were

categorized as chronic obstructive pulmonary disease, asthma, or pneumonia. The investigators analyzed lag patterns for exposure to each  ${\rm PM}_{2.5}$  constituent and hospital admissions for the six cardio-vascular and respiratory illnesses on the day of admission and each of 14 days prior.

On average there were 236 nonelective hospital admissions per day; 19% of these patients had a discharge diagnosis of cardiovascular disease, and 16% had a discharge diagnosis of respiratory disease. Cardiovascular hospital admissions were most strongly associated with a lag of 0–1 day, with the pattern most dominant for EC and OC, and for ischemic heart disease. Respiratory hospital admissions were most strongly associated with a longer lag of 2–5 days, with the pattern again most dominant for EC and OC, and with asthma showing the strongest associations. Sulfate and nitrate showed less association with any diagnosis at any lag. Lag patterns were consistent after adjusting for exposure to the gaseous copollutants carbon monoxide, sulfur dioxide, nitrogen dioxide, and ozone.

The study is limited by its reliance on only one residential monitoring site for ambient  $PM_{2.5}$  and its chemical constituents, but the authors write that the strong correlations between the data obtained from that site and from a nearby federal monitoring site support the validity of the study design. The authors plan future studies to explore whether specific sources of  $PM_{2.5}$  exhibit similar time lag effects.

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